

JAN 03 2011

Amendments to the Specification

Please replace the paragraph beginning at page 5, line 4, with the following rewritten paragraph:

In one embodiment of the present invention ~~[[invention]]~~, DNA hybridization on a silica microsphere surface is quantified from the red-shift of an optical resonance wavelength. The present invention may use the fact that the fractional shift of a resonance wavelength  $\delta\lambda/\lambda$  may be expressed as  $\alpha_{\text{ex}}\sigma_s/[\epsilon_0(n_s^2-n_b^2)R]$ , where  $\epsilon_0$  is the vacuum permittivity,  $R$  is the microsphere radius (200  $\mu\text{m}$ ),  $n_s$  (1.467) and  $n_b$  (1.332) are the refractive indices of the microsphere and the buffer solution, respectively.  $\alpha_{\text{ex}}$  is the excess polarizability (the polarizability of a volume of DNA (or some other target nucleotide chain) in excess of an equal volume of water) and  $\sigma_s$  is the surface density of the bound DNA (or other target nucleotide chain) ~~[[+]]~~ to determine the surface density of bound DNA target molecules.

Please replace the paragraph beginning at page 8, line 6, with the following rewritten paragraph:

The light source 120 may be a laser diode, such as a tunable, distributed feedback laser diode (e.g., 1312.8 nm nominal wavelength, 5 mW, ML776H11F from Mitsubishi of Japan). The optical fiber 110 may be a single mode optical fiber such as smf-28 optical fiber (e.g., from Canadian Instrumentation & Research Ltd. of Ontario, Canada). The detector 130 may be an InGaAs photodetector (e.g., PDA400, from Thorlabs of Newton,

NJ). The microspheres 140,150 may be silica microspheres evanescently coupled to the fiber 110.

Please replace the paragraph beginning at page 9, line 20, with the following rewritten paragraph:

The use of a microspheres to detect a substance, as well as fabrication of such microsphere-based detection systems and their components are described in: U.S. Patent Application Serial No. 10/096,333 (referred to as "the '333 application" and incorporated herein by reference), issued as U.S. Patent No. 7,491,491 on February 7, 2009, titled "DETECTING AND/OR MEASURING A SUBSTANCE BASED ON A RESONANCE SHIFT OF PHOTONS ORBITING A MICROSPHERE," filed on February 12, 2002, and listing Stephen Arnold and Iwao Teraoka as inventors; U.S. Patent Application Serial No. 10/690,979 (referred to as "the '979 application" and incorporated herein by reference), titled "ENHANCING THE SENSITIVITY OF A MICROSPHERE SENSOR," filed on October 22, 2003 and listing Stephen Arnold, Iwao Teraoka and Frank Vollmer as inventors; and U.S. Patent Application Serial No. 10/735,247 (referred to as "the '247 application" and incorporated herein by reference), titled "USING A CHANGE IN ONE OR MORE PROPERTIES OF LIGHT IN ONE OR MORE MICROSPHERES FOR SENSING CHEMICALS USHC AS EXPLOSIVES AND POISON GASES," filed on December 12, 2003 and listing Stephen Arnold, Iwao Teraoka, Yoshiyuki Okamoto and Frank Vollmer as inventors. Each of the foregoing applications is incorporated herein by reference. As will be appreciated by those skilled in the art, various teachings from those applications can be used in concert with the present invention.

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 Claim 1 (currently amended): For use in a system including  
2 a light source, and a light detector, for measuring ~~[[one~~  
3 ~~or more of at least two]]~~ a target substance ~~[[substances,~~  
4 ~~each of the at least two target substances]]~~ including a  
5 chain of nucleotides, a sensor comprising:  
6 a) at least one optical carrier;  
7 b) at least two optical cavities, wherein each of the  
8 at least two optical cavities is ~~[[1) being]]~~  
9 optically coupled with the optical carrier, ~~[[and]]~~  
10 wherein a first of the at least two optical cavities  
11 has ~~[[2) having]]~~ a surface including first  
12 oligonucleotides complementary to ~~[[a particular one~~  
13 ~~of the at least two]]~~ the target substance  
14 ~~[[substances]]~~, and wherein a second of the at least  
15 two optical cavities has a surface including second  
16 oligonucleotides complementary to a second  
17 oligonucleotide having only a single nucleotide  
18 mismatch with the target substance,  
19 wherein, when light is applied to the optical  
20 carrier, a resonance within each of the optical cavities is  
21 excited,  
22 wherein, if a target substance hybridizes with  
23 oligonucleotides on the surface of an optical cavity, a  
24 shift in the resonance of that optical cavity occurs, and  
25 wherein a measurement of the target substance can  
26 be determined based on the shift in resonance.

1 Claim 2 (original): The sensor of claim 1 wherein the  
2 optical carrier is an optical fiber.

1 Claim 3 (original): The sensor of claim 1 wherein at least  
2 one of the optical cavities is a microsphere.

1 Claim 4 (original): The sensor of claim 1 wherein at least  
2 one of the optical cavities is a toroidal microcavity.

1 Claim 5 (currently amended): The sensor of claim 1 wherein  
2 at least one of the optical cavities is an Indium Phosphide  
3 ~~[[a-InP]]~~ microdisk.

1 Claim 6 (currently amended): The sensor of claim 1 wherein  
2 ~~[[at least one of]]~~ the first oligonucleotides are  
3 complementary to a target ~~[[substances is]]~~ DNA.

1 Claim 7 (currently amended): The sensor of claim 1 wherein  
2 ~~[[at least one of]]~~ the first oligonucleotides are  
3 complementary to a target ~~[[substances is]]~~ RNA.

1 Claim 8 (original): The sensor of claim 1 wherein, if a  
2 target substance hybridizes with oligonucleotides on the  
3 surface of an optical cavity surface, a shift in the  
4 resonance of that optical cavity of a first amount occurs,  
5 and  
6 wherein if a substance which differs from the target  
7 substance by a single nucleotide is made available for  
8 hybridization with the surface of the optical cavity  
9 surface, a shift in the resonance of the optical cavity of  
10 a second amount occurs, wherein the first amount is  
11 detectably greater than the second amount.

1 Claim 9 (original): The sensor of claim 8 wherein the

2 first amount is at least ten times greater than the second  
3 amount.

1 Claim 10 (original): The sensor of claim 1 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are 11-mer oligonucleotides.

1 Claim 11 (original): The sensor of claim 1 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are at least 27-mer oligonucleotides.

1 Claim 12 (original): The sensor of claim 1 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are at least 11-mer oligonucleotides.

1 Claim 13 (original): The sensor of claim 1 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are at most 27-mer oligonucleotides.

1 Claim 14 (currently amended): A system for measuring one  
2 or more of at least two target substances, each of the at  
3 least two target substances including a chain of  
4 nucleotides, the system comprising:  
5 a) a light source;  
6 b) a light detector;  
7 c) a sensor, the sensor including  
8 1) at least one optical carrier optically  
9 coupled with both the light source and the light  
10 detector;  
11 2) at least two optical cavities, each of the at  
12 least two optical cavities  
13 A) being optically coupled with the optical

14 carrier, and  
15 B) having a surface including  
16 oligonucleotides complementary to a  
17 particular one of the at least two target  
18 substances,  
19 wherein, when the light source applies  
20 light to the optical carrier, a resonance within  
21 each of the optical cavities, having a first  
22 characteristic, is excited and is detected by the  
23 detector, and  
24 wherein, if a target substance  
25 hybridizes with oligonucleotides on the surface  
26 of an optical cavity, a change in the  
27 characteristic of the resonance of that optical  
28 cavity occurs and is detected by the light  
29 detector; and  
30 d) a processor for determining a measurement of the  
31 target substance using a difference [[a-shift]] in  
32 shifts between the [[characteristic of the]]  
33 resonances detected by the light detector.

1 Claim 15 (original): The system of claim 14 wherein the  
2 optical carrier is an optical fiber.

1 Claim 16 (original): The system of claim 14 wherein at  
2 least one of the optical cavities is a microsphere.

1 Claim 17 (original): The system of claim 14 wherein at  
2 least one of the optical cavities is a toroidal  
3 microcavity.

1 Claim 18 (currently amended): The system of claim 14

2 wherein at least one of the optical cavities is an Indium  
3 Phosphide ~~[[a-InP]]~~ microdisk.

1 Claim 19 (currently amended): The system of claim 14  
2 wherein ~~[[at least one of]]~~ the oligonucleotides are  
3 complementary to a target ~~[[substances is]]~~ DNA.

1 Claim 20 (currently amended): The system of claim 14  
2 wherein ~~[[at least one of]]~~ the oligonucleotides are  
3 complementary to a target ~~[[substances is]]~~ RNA.

1 Claim 21 (original): The system of claim 14 wherein, if a  
2 target substance hybridizes with oligonucleotides on the  
3 surface of an optical cavity surface, a shift in the  
4 resonance of that optical cavity of a first amount occurs,  
5 and  
6 wherein if a substance which differs from the target  
7 substance by a single nucleotide is made available for  
8 hybridization with the surface of the optical cavity  
9 surface, a shift in the resonance of the optical cavity of  
10 a second amount occurs, wherein the first amount is  
11 detectably greater than the second amount.

1 Claim 22 (original): The system of claim 21 wherein the  
2 first amount is at least ten times greater than the second  
3 amount.

1 Claim 23 (original): The system of claim 14 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are 11-mer oligonucleotides.

1 Claim 24 (original): The system of claim 14 wherein the

2 oligonucleotides provided on at least one of the optical  
3 cavities are at least 27-mer oligonucleotides.

1 Claim 25 (original): The system of claim 14 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are at least 11-mer oligonucleotides.

1 Claim 26 (original): The system of claim 14 wherein the  
2 oligonucleotides provided on at least one of the optical  
3 cavities are at most 27-mer oligonucleotides.

1 Claim 27 (original): The system of claim 14 wherein the  
2 processor determines the measurement of the target  
3 substance using a shift in characteristic of the resonances  
4 detected by the detector, and refractive indices of the  
5 optical cavity and a solution in which the target substance  
6 is allowed to come into contact with the optical cavity.

1 Claim 28 (original): The system of claim 27 wherein the  
2 processor determines the measurement of the target  
3 substance further using an excess polarizability of a  
4 volume of the target over an equal volume of a solution in  
5 which the target is provided.

1 Claim 29 (original): The system of claim 14, wherein the  
2 optical cavity is a microsphere, and  
3 wherein the processor determines the measurement of  
4 the target substance using a shift in characteristic of the  
5 resonances detected by the detector, and a radius of the  
6 microsphere.

1 Claim 30 (original): The system of claim 14 wherein the



2 measurement of the target substance is a surface density of  
3 the target substance bound to the optical cavity.

1 Claim 31 (original): The system of claim 14 wherein the at  
2 least one optical carrier includes a plurality of optical  
3 fibers.

1 Claim 32 (original): The system of claim 31 wherein each  
2 of the plurality of optical fibers is optically coupled  
3 with at least two of the optical cavities:

1 Claim 33 (original): The system of claim 31 further  
2 comprising at least one additional light detector,  
3 wherein at least two of the plurality of optical fibers  
4 are optically coupled with a common light source, but with  
5 different light detectors.

Claims 34-39 (canceled)

1 Claim 40 (new): The sensor of claim 1 further comprising:  
2 c) two substantially parallel substrates  
3 accommodating each of the at least two optical  
4 cavities.

1 Claim 41 (new): The sensor of claim 40 wherein the at  
2 least one optical carrier is arranged between the two  
3 substantially parallel substrates.